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# Integrative Oncology: A Paradigm Shift

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# Integrative Oncology: A Paradigm Shift



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# Disclosures

- I do not have any relevant financial relationships to disclose at this time.



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## Integrative Medicine

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[Individual Therapies](#)

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**Integrative oncology physician consultation**



**Acupuncture**



**Exercise and physical activity consultations**



**Health psychology**



**Meditation**



**Music therapy**



**Nutrition counseling**



**Oncology massage**



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# Integrative Medicine @ MCI

- Integrative Oncology Consultation
  - Oncology Acupuncture
  - Oncology Massage
  - Nutritional counseling – by RD nutritionist
  - Exercise Physiology
  - Yoga for Cancer
- Referral
  - Psychosocial Oncology – by psychiatrists
  - Survivorship
  - Social Work Services
  - Pastoral Care
  - Palliative Care



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# Conditions Treated:

- Conditions treated:
  - Nausea
  - Pain
  - Fatigue
  - Emotional distress
  - Xerostomia,
  - Chemotherapy Induced Peripheral Neuropathy
  - Chemotherapy Induced Cognitive Impairment



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# Integrative Oncology

- Among patients employing complementary therapies, few divulge this information to their treating oncologist (Tasaki, 2002).
- More recent article shows that most patients use herbs during active treatment & completely unsupervised by any professional (alternative or integrative) (Powell 2002).
  - Tasaki, Katsuya, et al. "Communication between physicians and cancer patients about complementary and alternative medicine: exploring patients' perspectives." *Psycho-Oncology* 11.3 (2002): 212-220.
  - Powell, C. B., et al. "Use of herbs in women diagnosed with ovarian cancer." *International Journal of Gynecological Cancer* 12.2 (2002): 214-217.



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# Case Report 1

- Doctor, my husband has serious cancer (brain cancer), can I use serious herb?
  - Herb the patient's spouse had in mind was wolf's bane or aconite.



• Photo Credit: Wikipedia



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# Woman, 56, dies after drinking toxic tea from SF Chinatown shop

A San Francisco woman named Yu-Ping Xie died after consuming toxic tea from an herbal remedy shop in Chinatown. Within an hour of drinking the tea, she and an unidentified male victim experienced weakness and irregular heart rhythms. Aconite, a deadly plant-based toxin, was found in traces of the tea and in the victims' lab tests. It is used in Asian herbal tea remedies and is known to have healing qualities, but if left unprocessed it can pose fatal risks. The city's health officials are warning residents to stay clear of the company that sells the tea products, and that there is no antidote for the toxin.

If prepared properly, aconite is said to have anti-inflammatory properties and has long been used in traditional Chinese medicine. But the purple flower in its raw state — also called wolf's bane, monkshood and helmet flower — can be a deadly cardiotoxin.



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# Case Report 1

- Please stop ALL supplements
- Education:
  - All supplements (even “liver protective”) have to be processed by liver
  - Not a best time for patients to increase work load of the liver
  - Lifestyle medicine + Acupuncture/Massage for symptomatic relief



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# Integrative Medicine in Cancer Patients

- Integrative Oncology
  - Emphasize lifestyle choices (food, physical activity, mind-body medicine) over supplements.
  - Choice of herbs/supplements based on current evidenced based risk/benefit assessment
  - Communicate with other physicians/providers and complement on-going cancer treatment



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# Integrative Oncology Key Issues

- Potential drug-CAM therapy interaction
  - When patients ask about CAM, blind prohibition by non-integrative medicine physician - likely result in utilizing CAM without communication.
  - We can use the best available evidence to make mindful recommendations to our patients seeking CAM.



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# Case Report 2

- “I know I have a serious illness (B cell CLL; developed severe side effect to Rituxan) – I know the cancer is not gone so I am taking 30 supplements”
  - Source of supplement is his best friend without any health care background
- Outcome: agreed to drink up to 6 cups of green tea and curcumin 500 mg TID



# Case Report



**NIH Public Access**

**Author Manuscript**

*Clin Cancer Res.* Author manuscript; available in PMC 2010 February 15.

Published in final edited form as:

*Clin Cancer Res.* 2009 February 15; 15(4): 1123–1125. doi:10.1158/1078-0432.CCR-08-2791.

## **Turmeric and green tea: a recipe for B-Chronic Lymphocytic Leukemia**

**Laura S. Angelo and Razelle Kurzrock**

### **Summary**

Two naturally-occurring compounds--curcumin (the active ingredient in the spice turmeric) and the green tea extract epigallocatechin-3-gallate (EGCG) have marked effects on the apoptotic machinery in chronic lymphocytic leukemia (CLL). These results provide a preclinical foundation for future clinical use of these compounds in this disease.



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# Integrative Oncology Key Issues

- The evidence supporting “alternative” cancer treatments either
  - Evidence is absent.
  - Evidence shows lack of effectiveness.
- Educating our patient rather than “alternative,” utilize integrative medicine for what is shown to be effective – effective symptom relief using safe, natural modalities of healing
- Allows for posing questions to explore new topics such as can curcumin play a role for treating cancer



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# Common Myths – nature = safe?

- Vitamin ABCED –
  - Vitamin A
    - 18% increased risk of lung CA (high dose beta-carotene)
    - 28% increased risk of lung CA (beta-carotene and retinol)
  - Vitamin B
    - No effect – Vitamin B2 (riboflavin), B3 (niacin) on upper GI cancers
    - Folic acid (vitamin B9) → increased colorectal adenomas
  - Vitamin C
    - No effect on gastric cancer rate





# Common Myths – nature = safe?

- Vitamin ABCED –

- Vitamin E

- Slight increase in overall mortality
    - Vitamin E + Selenium – no effect on reducing prostate cancer

- Vitamin D

- Vitamin D Pooling Project of Rarer Cancers

- Vitamin D levels not reduce risk of rarer cancers (upper GI, ovary, endometrial, pancreatic, kidney, and non-Hodgkin lymphoma)

- Highest quintile of vitamin D level → pancreatic cancer risk 2x

- Byers T. Anticancer Vitamins du Jour – The ABCED's so Far. Am J Epidemiol. 2010. 172:1-3



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# ACS Life Style Recommendations

- Be as lean; avoid excess weight
- Regular physical activity (150 min. moderate intensity per week)
- Limit sedentary behavior
- Limit high calorie food & drinks
- Limit consumption of processed meat and red meat
- Eat > 2.5 cups of vegetables and fruits every day
- Choose whole grains
- Max 1 drink per day for women; 2 per day for men
- Kushi, Lawrence H., et al. "American Cancer Society Guidelines on Nutrition and Physical Activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity." *CA: a cancer journal for clinicians* 56.5 (2006): 254-281.



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# Lifestyle Recommendations

- WCRF/AICR Recommendation on Dietary Supplements
  - Dietary supplements are not recommended for cancer prevention
  - Aim to meet nutritional needs through diet alone
- World Cancer Research Foundation
- American Institute of Cancer research



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# First Do No Harm... primum non nocere

- SELECT study
  - Vitamin E + Selenium for reduction of prostate cancer study
    - Early termination due to increased risk of prostate cancer in vitamin E group (Lippman 2009)
    - Addition follow up study confirmed finding Klein 2011)
- Folic acid + B12 also shown to increase the risk of cancer and cancer related mortality (Ebbing 2009)
  - Lippman, Scott M., et al. "Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT)." *Jama* 301.1 (2009): 39-51.
  - Ebbing, Marta, et al. "Cancer incidence and mortality after treatment with folic acid and vitamin B12." *Jama* 302.19 (2009): 2119-2126.



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# CAM-Chemo Interactions

- Supplement-Pharmaceutical Interaction
  - Cytochrome P450 modulated
  - CYP 3A4 mediated meds
    - Camptothecins, cyclophosphamide, epipodophyllotoxins, vica alkaloids, taxane, EGFR inhibitors
  - CYP 3A4 inducing herbs (decrease concentration and efficacy of cancer tx)
    - St. John's wort, Echinacea\*, grape seed, kava, garlic
  - CYP 3A4 inhibition (increase concentration of chemo)
    - Gingko and Goldenseal



# Antioxidant Debate

- A systematic review of 19 RCT reporting survival and/or tumor response involved 1552 patients on various anti-oxidants. (Block 2008)
  - Antioxidants
    - Glutathione, melatonin, vit A, mixture of anti-oxidant, vit C, N-acetylcysteine, vit E
    - 17 of 19 RCT showed – significant advantage or statistically non-significant increase in survival or treatment response\*
    - No diminished chemotherapy effect
    - Block, Keith I., et al. "Impact of antioxidant supplementation on chemotherapeutic toxicity: a systematic review of the evidence from randomized controlled trials." *International Journal of Cancer* 123.6 (2008): 1227-1239.



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# Anti-oxidant Debate Continued...

- Mesna (Mesnex) – medication used in those taking cyclophosphamide or ifosfamide to decrease the risk of bleeding from the bladder.
  - Anti-oxidant – organosulfur compound
    - Others include lipoic acid, penicillin, sulfonamide, allicin (crushed garlic), cysteine, methionine, etc.



# Anti-oxidant debate continued

- Amifostine (Ethiofos) – medication to reduce incidence of neutopenia and to decrease cumulative nephrotoxicity associated with platinum containing agents. Also to reduce xerostomia in patients undergoing head and neck cancer radiation therapy
  - Organic thiophosphate prodrug → cytoprotective thiol metabolite (scavenges free radicals – detoxified reactive metabolites)



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# Anti-oxidant Recommendation

- Evidence – “first do no harm” is not met with vitamin studies
- Obtaining anti-oxidant through food – by eating a “rainbow” diet appears to be most safest approach.
- Integrative Medicine often makes use of anti-inflammatory diet which is rich in anti-oxidants and anti-inflammatory agents.



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# Omega-3 fatty acids

- SELECT trial analysis (Brasky 2013)
    - Higher level of plasma omega-3 EFA at increased risk for more aggressive prostate cancer
  - (Aronson 2011)
    - Omega-3 EFA (5 grams) + low fat intake (15%)
    - Smaller, less aggressive forms of cancer
  - (Murphy 2011)
    - Omega-3 EFA + Chemo regimen
    - Better outcomes – were able to receive more chemo
    - Survival was not different
- Brasky, Theodore M., et al. "Plasma phospholipid fatty acids and prostate cancer risk in the SELECT trial." *Journal of the National Cancer Institute* 105.15 (2013): 1132-1141.
- Aronson, William J., et al. "Phase II prospective randomized trial of a low-fat diet with fish oil supplementation in men undergoing radical prostatectomy." *Cancer prevention research* 4.12 (2011): 2062-2071.
- Murphy, Rachel A., et al. "Supplementation with fish oil increases first-line chemotherapy efficacy in patients with advanced nonsmall cell lung cancer." *Cancer* 117.16 (2011): 3774-3780.



# VITAL Study – On Going

- VIT D + Omega-3 Trial (2010 – ongoing)
  - 25,874 men and women in the US
  - Intervention
    - Vit D3 (2000 IU)
    - Omega-3 fatty acids (Omacor fish oil 1 g)
  - Outcome
    - Cancer, heart disease, stroke
    - Primary prevention
  - <http://www.vitalstudy.org/>



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# Supplements in Integrative Oncology

- Professional Consensus
  - Medicinal Mushroom Supplements
    - Reishi (*Ganoderma Lucidum*)
    - *Trametes versicolor*
    - Whole extract v. fractionated
  - Turmeric v. Curcumin \*/Quercetin/Bromelain
  - Astragalus
  - Melatonin
  - Milk thistle
  - Garlic
  - Mistletoe \*\*\* (Europe)



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# Case 3

- Patient with metastatic colon cancer who elects no further treatment to be done
  - Organic farmer
  - Compassionate Use of Integrative Medicine?
    - Initial supplement:
      - Curcumin 500 mg Q 2 hours x 6 while awake
      - Mushroom mixture: Stamets 7 1 pill Q 2 hours x 6 while awake
      - Patient to f/u with oncologist
      - I will follow patient with CBC CMP monthly
      - Target Curcumin 6 g per day – research dose
      - May consider single mushrooms – Reishi, Turkey Tail, Maitake



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# Stress Reduction

- Stress
  - Epinephrine → lymphocytotoxic
  - Cortisol → immunosuppressant
  - Newer studies show VEGF (vascular endothelial growth factor) & MMP-9 (associated with invasion and metastasis) higher in depressed women and lower in patients with higher social support.
    - Lutgendorf SK et al. Biobehavioral influences on matrix metalloproteinase expression in ovarian carcinoma. Clin Cancer Res. 14(21):6839-6846. Nov 1, 2008
    - Feng et al. Psychosocial functioning and vascular endothelial growth factor in patients with head and neck cancer. Head Neck 36(8):1113-1119 Aug 2014



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# Stress Reduction

- MBSR
  - Growing evidence on effectiveness for addressing fear, depression & anxiety, fatigue & sleep quality.
    - Eyles C et al. Mindfulness for the Self-Management of Fatigue, Anxiety, and Depression in Women With Metastatic Breast Cancer: A Mixed Methods Feasibility Study. Integr Cancer Ther 26 Aug 2014
    - Lengacher CA. The effects of mindfulness-based reduction on objective and subjective sleep parameters in women with breast cancer: a randomized controlled trial. Psychooncology 18 Jun 2014



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# The Value of Acupuncture in Cancer Care\*

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2642987/>

- Acupuncture Oncology - how it differs from community acupuncture
- Focuses on protocols developed from research trials rather than traditional approach
- Evidence, reliability and validity over traditional “energetic” treatments





# Contraindication Acupuncture

- ANC less than 1000
- Platelet count less than 25,000
  - However, no bleeding issues related to use of acupuncture even with severe thrombocytopenia (less than 20,000)
    - Ladas et al. The safety of acupuncture in children and adolescent with cancer therapy related thrombocytopenia. Support Care Cancer. 18(11):1487-90 June 18 2010



## Patient's Perspective on Integrative Oncology

<https://integrativeonc.org/docman-library/journal-articles/153-josh-mailman-j-natl-cancer-inst-monogr-2014-mailman-291/file>

## Clinical Practice Guidelines on the Use of Integrative Therapies as Supportive Care in Patients Treated for Breast Cancer

<http://jncimono.oxfordjournals.org/content/2014/50/346.full.pdf+html>



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Services limited to MCI cancer patients



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# Additional References:

- University of Arizona – Center for Integrative Medicine – Integrative Oncology Section.
- SF Gate ([www.sfgate.com](http://www.sfgate.com))



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